I hereby certify that this correspondence is being hand-delivered to: Examiner Teresa D. Wessendorf/ Examiner Andrew J. Wang United States Patent and Trademark Office

Art Unit 1639 1911 S. Clark Place Crystal Mall One, 7th Floor Arlington, VA 22202 703-308-3967

Printed Name:

Attorney Docket No. 0155.130US (formerly 18097-030310US)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Juha Punnonen et al.

Application No.: 09/724,869

Filed: November 28, 2000

For: **OPTIMIZATION OF**

> **IMMUNOMODULATORY** PROPERTIES OF GENETIC

VACCINES

SECOND SUPPLEMENTAL **INFORMATION DISCLOSURE** STATEMENT UNDER 37 CFR §§ 1.97 **AND 1.98**

Examiner: Teresa D. Wessendor:

Art Unit: 1639

Examiner Teresa D. Wessendorf Examiner Andrew J. Wang United States Patent and Trademark Office Art Unit 1639 1911 S. Clark Place Crystal Mall One, 7th Floor Arlington, VA 22202

Dear Madam/Sir:

The references cited on attached form PTO/SB/08A-B are being called to the attention of the Examiner. Copies of the references are enclosed. It is respectfully requested that the cited information be expressly considered during the prosecution of this application and the references be made of record therein and appear among the "references cited" on an patent to issue therefrom.

As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no 10,007,000 10,007

Application No. 09/724,869 Page 2

representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

A Fee Transmittal Form is submitted concurrently herewith, authorizing the Commissioner to deduct any required fee from, or credit any overpayment to, the undersigned's Deposit Account No. 50-0990.

Respectfully submitted,

October 8, 2003

Bv:

R. Danny Huntington Registration No. 27,903

Sharon E. Crane

Registration No. 36,113

Mercedes K. Meyer

Registration No. 44,939

Attorneys for Applicants

Maxygen, Inc.
Patent Department
515 Galveston Drive
Redwood City, California 94063
Telephone: (650) 298-5300

Facsimile: (650) 298-5446

Customer No. 30560

Substitute for form 1449A-B/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Complete if Known

Application Number 09/724,869

Filing Date November 28, 2000

First Named Inventor Juha Punnonen

Group Art Unit 1639

Examiner Name Teresa Wessendorf

Attorney Docket Number 0155.130US

(use as many sheets as necessary)

	U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	U.S. Patent Docu Number	ment Kind Code (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, lines, Where Relevant Passages or Relevant Figures Appeal
	1	6,376,246		Crameri et al.	04-09-2002	

				FOREIGI	N PATENT DOCUMEN	TS	
			Foreign Patent Docu		Name of Patentee or Applicant of Cited Document	Date of Publication	Pages, Columns, Lines,
Exami ner Initials	Cite No.	Office	Number	Kind Code (if known)		of Cited Document MM-DD-YYYY	Where Relevant Passages or Relevant Figures Appear
	2	wo	91/19818	A1	Affymax Technologies N.V.	12-26-1991	
	3	wo	92/01047	A1	Cambridge Antibody Technology Limited	01-23-1992	,
	4	wo	92/18619	A1	The Scripps Research Institute	10-29-1992	
	5	wo	94/01567	A1	Unilever PLC	01-20-1994	
	6	wo	94/18330	A1	Unilever PLC	08-18-1994	

		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS
Exami ner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
	7	Aggarwal & Gutterman eds., Human Cytokines: Handbook for Basic and Clinical Research, Vol. II (1996) (Table of Contents for Vols. 1 & II)
	8	Alcami <i>et al.</i> , "A soluble receptor for interleukin-1 beta encoded by vaccinia virus: a novel mechanism of virus modulation of the host response to infection," <i>Cell</i> 71(1):153-67 (1992)
	9	Apostolopoulos et al., "Breast cancer immunotherapy: Current status and future prospects," Immunol. and Cell. Biol. 74:457-64 (1996)
	10	Atamas et al., "An alternative splice variant of human IL-4, IL-4 delta 2, inhibits IL- 4-stimulated T cell proliferation," J. Immunol. 156(2):435-41 (1996)
	11	Aversa et al., "SLAM and its role in T cell activation and Th cell responses." Immunol. Cell Biol. 75(2):202-5 (1997)
	12	Bach et al., "The IFN gamma receptor: a paradigm for cytokine receptor signaling," Annu. Rev. Immunol. 15:563-91 (1997)
	13	Baggioloni et al., "Human Cytokines: An Update," Annu. Rev. Immunol. 15:675-705 (1997)
	14	Balbas et al., "Design and Construction of Expression Plasmid Vectors in Escherichia coli," in METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY 185:14-37 (David V. Goeddel ed., Acad. Press, Inc., 1990)
	15	Basham et al., "Synergistic antitumor activity with IFN and monoclonal anti-idiotype for murine B cell lymphoma. Mechanism of action," J. Immunol. 141(8):2855-60 (1988)
	16	Beck et al., "Analysis of Multiple Plasmodium falciparum Infections in Tanzanian Children during the Phase II Trial of Malaria Vaccine SPf66," J. Inf. Disease 175:921-26 (1997)

(Modified) PTO/SB/08A-B (10-96) Approved for use through 10/31/99. OMB 0651-0031 Application No.: 09/724,869

Application No.: 09/724,869 Filing Date: November 28, 2000 First Inventor: Juha Punnonen Art Unit: 1639

Examiner Name: Teresa Wessendorf Attorney Docket No.: 0155.130US

17	Becket et al., "Characterization of a Prostate Carcinoma Mucin-Like Antigen (PMA)," Int. J. Cancer 62:703-10 (1995)
18	Bramson et al., "Construction of a double recombinant adenovirus vector expressing a heterodimeric cytokine: in vitro and in vivo production of biologically active interleukin-12," Hum. Gene Ther. 7(3):333-42 (1996)
19	Brusselle <i>et al.</i> , "Role of IFN-γ in the Inhibition of Allergic Airway Inflammation Caused by IL-12," <i>Am. J. Respir. Cell Mol. Biol.</i> 17:767-71 (1997)
20	Censini et al., "cag, a pathogenicity island of Helicobacter pylori, encodes type I-specific and disease-associated virulence factors," PNAS 93:14648-53 (1996)
21	Chen et al., "Discontinuous epitopes of hepatitis B surface antigen derived from a filamentous phage peptide library," PNAS USA 93(5):1997-2001 (1996)
22	Chow et al., "Improvement of Hepatitis B Virus DNA Vaccines by Plasmids Coexpressing Hepatitis B Surface Antigen and Interleukin-2," J. Virol. 71(1):169-78 (1997)
23	Ciernik et al., "Induction of Cytotoxic T Lymphocytes and Antitumor Immunity with DNA Vaccines Expressing Single T Cell Epitopes," J. Immunol. 156:2369-75 (1996)
24	Cohen et al., "Host factors in the pathogenesis of HIV disease," Immunol. Rev. 159:31-48 (1997)
25	Cortese et al., "Selection of biologically active peptides by phage display of random peptide libraries," Curr. Opin. Biotechnol. 7(6):616-21 (1996)
26	Curtis et al., "Recombinant Soluble Interleukin-11 (IL-11) Receptor alpha Chain Can Act as an IL-11 Antagonist," Blood 90(11):4403-12 (1997)
27	Cwirla et al., "Peptide Agonist of the Thrombopoietin Receptor as Potent as the Natural Cytokine," Science 276:1696-9 (1997)
28	Dagan et al., "High level expression and production of recombinant human interleukin analogs," Protein Expr. Purif. 3(4):290-4 (1992)
29	Devos et al., "Interleukin-5 and its receptor: a drug target for eosinophilia associated with chronic allergic disease," J. Leukoc. Biol. 57(6):813-19 (1995)
30	De Vries et al., "Novel fundamental approaches to intervening in IgE-mediated allergic diseases," J. Invest. Dermatol. 102(2):141-4 (1994)
31	De Vries et al., Interleukin-4 and Interleukin-13, Chap. 8, in CYTOKINE REGULATION OF HUMORAL IMMUNITY: BASIC AND CLINICAL ASPECTS 195-215 (C. M. Snapper, West Sussex, UK, John Wiley and Sons, 1996)
32	De Vries et al., "Modulation of the human IgE response," Eur. Respir. J. Suppl. 22:58s-62s (1996)
33	De Waal Malefyt et al., "A Novel Cytokine Belonging to the IL-10 Gene Family Affects Human Monocytes and T Cells," Abstract, 13th European Immunology Meeting, Amsterdam, Netherlands, June 1997, Immunol. Letters 56(1):211 (May 1997)
34	Donnelly et al., "DNA Vaccines," Annu. Rev. Immunol. 15:617-48 (1997)
35	Dudler et al., "A Link Between Catalytic Activity, IgE-Independent Mast Cell Activation and Allergenicity of Bee Venom Phospholipase A ₂ ," J. Immunol. 155(5):2605-13 (1995)
36	Eckhart et al., "Immunogenic presentation of a conserved gp41 epitope of human immunodeficiency virus type 1 on recombinant surface antigen of hepatitis B virus," J. Gen. Virol. 77 (9):2001-8 (1996)
Examiner	Date
Signature	Considered
	<u> </u>

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

(Modified) PTO/SB/08A-B (10-96) Approved for use through 10/31/99. OMB 0651-0031

Application No.: 09/724,869 Filing Date: November 28, 2000 First Inventor: Juha Punnonen

Art Unit: 1639

Examiner Name: Teresa Wessendorf Attorney Docket No.: 0155.130US

37	Fomsgaard et al., "Improved humoral and cellular immune response against the gp120 V3 loop of HIV-1 following genetic immunization with a chimeric DNA vaccine encoding the V3 inserted in the hepatitis B surface antigen," Scand. J. Immunol. 47(4):289-95 (1998)		
38	Foy et al., "Immune regulation by CD40 and its ligand GP39," Annu. Rev. Immunol. 14:591-617 (1996)		
39	Fromm et al., "Expression of genes transferred into monocot and dicot plant cells by electroporation." PNAS USA 82(17):5824-28 (1985)		
40	Gauchat et al., "Regulation of human IgE synthesis: the role of CD4+ and CD8+ T-cells and the inhibitory effects of interferon-alpha." Eur. Respir. J. Suppl. 13:31s-38s (1991)		
41	Goff et al., "Laboratory Methods: Efficient Saturation Mutagenesis of a Pentapeptide Coding Sequence Using Mixed Oligonucleotides," DNA 6(4):381-388 (1987)		
42	Greenfeder et al., "Insertion of a Structural Domain of Interleukin (IL)-1B Confers Agonist Activity to the IL-1 Receptor Antagonist," J. Biol. Chem. 270:22460-6 (1995)		
43	Grewal et al., "The CD40-CD154 system in anti-infective host defense," Curr. Opin. Immunol. 9(4):491-7 (1997)		
44	Grunig et al., "Interleukin-10 is a natural suppressor of cytokine production and inflammation in a murine model of allergic bronchopulmonary aspergillosis." J. Exp. Med. 185(6):1089-99 (1997)		
45	Hannum et al., "Interleukin-1 receptor antagonist activity of a human interleukin-1 inhibitor," Nature 343:336-40 (1990)		
46	Hathcock et al., "Comparative Analysis of B7-1 and B7-2 Costimulatory Ligands: Expression and Function," J. Exptl. Med. 180:631-40 (1994)		
47	Herz et al., "Molecular approaches to receptors as targets for drug discovery," J. Recept. Signal Transduct. Res. 17(5):671-776 (1997)		
48	Herzenberg et al. eds., WEIR'S HANDBOOK OF EXPERIMENTAL IMMUNOLOGY (5 th ed. 1996) (index and first pages of Chaps. 220, 226, 227)		
49	Hess et al., "Superior efficacy of secreted over somatic antigen display in recombinant Salmonella vaccine induced protection against listeriosis," PNAS 93:1458-63 (1996)		
50	Hill et al., "Mutagenesis with Degenerate Oligonucleotides: An Efficient Method for Saturating a Defined DNA Region with Base Pair Substitutions," in METHODS IN ENZYMOLOGY: RECOMBINANT DNA 155:558-568 (Ray Wu ed., Acad. Press, Inc., 1987)		
51	Horuk, "Molecular properties of the chemokine receptor family," TIPS 15:159-165 (1994)		
52	Horwitz et al., "Saturation Mutagenesis Using Mixed Oligonucleotides and M13 Templates Containing Uracil," in METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY 185:599-611 (David V. Goeddel ed., Acad. Press, Inc. 1990)		
53	Ihle et al., "Signaling through the hematopoietic cytokine receptors," Annu. Rev. Immunol. 13:369-98 (1995)		
54	Kaufman, "Vectors Used for Expression in Mammalian Cells," in METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY 185:487-511 (David V. Goeddel ed., Acad. Press, Inc., 1990)		
55	Kay et al., eds., Phage Display of Peptides and Proteins: A Laboratory Manual (Acad. Press, Inc., 1996) (first page of Chap. 5)		
56	Krieger et al., "Structures and functions of multiligand lipoprotein receptors: macrophage scavenger receptors and LDL receptor-related protein (LRP)," Annu. Rev. Biochem. 63:601-		
Examiner	Date		
Signature	Considered		

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

(Modified) PTO/SB/08A-B (10-96) Approved for use through 10/31/99. OMB 0651-0031

Application No.: 09/724,869 Filing Date: November 28, 2000 First Inventor: Juha Punnonen

Art Unit: 1639

Examiner Name: Teresa Wessendorf Attorney Docket No.: 0155.130US

	37 (1994)		
57	Kroemer et al., "Immunoregulation by cytokines," Cr	rit. Rev. Immunol. 1	3(2):163-91 (1993)
58	Laberge et al., "Secretion of IL-16 (Lymphocyte Che Stimulated CD8 ⁺ T Cells In Vivo," J. Immunol. 156(1):310-5 (1996)	
59	Le Borgne et al., "In Vivo Induction of Specific Cytot Macaques Immunized with DNA Vector Encoding an Surface Antigen," Virology 240:304-15 (1998)	n HIV Epitope Fuse	ed with Hepatitis B
60	Le Grice, "Regulated Promoter for High-Level Expresubtilis," in METHODS IN ENZYMOLOGY: GENE EXPRESUGOED GOED Ed., Acad. Press, Inc., 1990)	SION TECHNOLOGY	185:201-15 (David V.
61	Levinson, "Expression of Heterologous Genes in Ma ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY 185:4 Press, Inc., 1990)		
62	Livnah et al., "Functional Mimicry of a Protein Horme Receptor Complex at 2.8," Science 273:464-71 (199		gonist: The EPO
63	Ma et al., "Antibody production and engineering in p (1996)		ad. Sci. 792:72-81
64	Mattion et al., "Characterization of recombinant policy VP4, hepatitis B surface antigen, and herpes simple 69:5132-37 (1995)	ex virus type 2 glyc	oprotein D," J. Virol.
65	McLafferty et al., "M13 bacteriophage displaying dis 128(1):29-36 (1993)	ulfide-constrained	microproteins," Gene
66	Miele, "Plants as bioreactors for biopharmaceuticals: regulatory considerations," <i>Trends Biotechnol.</i> 15(2):45-50 (1997)		
67	Mosmann et al., "Heterogeneity of Cytokine Secretion Patterns and Functions of Helper T cells," Adv. Immunol. 46:111-147 (1989)		
68	Murray et al., "Saturation mutagenesis of a major his Identification of a single conserved amino acid impo 85:3535-39 (1988)		
69	Noguchi et al., "IgE responsiveness to Dermatophas IgE binding study using recombinant allergens of De f2," Int. Arch. Allergy Immunol. 110(4):380-7 (1996)		
70	Ostermeier et al., "A combinatorial approach to hybrid homology," Nature 19:1205-09 (1999)	-	
71	Ostermeier et al., "Combinatorial protein engineering 96:3562-67 (1999)	g by incremental tr	uncation," PNAS USA
72	Parronchi et al., "IL-4 and IFN (alpha and gamma) e development of cytolytic potential by Th1 or Th2 hur 149(9):2977-83 (1992)	man T cell clones,"	J. Immunol.
.73	Paul, The Immune System: An Introduction, Chap. (W. E. Paul. New York, Raven Press, 1993)		
74	Porcelli, "The CD1 family: a third lineage of antigen- 59:1-98 (1995)	presenting molecu	les," Adv. Immunol.
xaminer		Date	
Signature		Considered	

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

(Modified) PTO/SB/08A-B (10-96) Approved for use through 10/31/99. OMB 0651-0031

Application No.: 09/724,869 Filing Date: November 28, 2000 First Inventor: Juha Punnonen

Art Unit: 1639

Examiner Name: Teresa Wessendorf Attorney Docket No.: 0155.130US

75	Pumpens <i>et al.</i> , "Hepatitis B virus core particles as epitope carriers," <i>Intervirology</i> 38(1-2):63-74 (1995)	
76	Quaratino et al., "Similar antigenic surfaces, rather than sequence homology dictate T-cell epitope molecular mimicry," PNAS USA 92:10398-402 (1995)	,
77	Randhawa et al., "In vitro culture of B-lymphocytes derived from Epstein-Barr-virus-associated posttransplant lymphoproliferative disease: cytokine production and effect of interferon-alpha," In Vitro Cell Dev. Biol. Anim. 33(10):803-08 (1997)	
78	Sambrook <i>et al.</i> , MOLECULAR CLONING: A LABORATORY MANUAL, Cold Spring Harbor Laboratory Press, New York (2d ed. 1989), Vol. I, pp. 1.53-1.59	,
79	Sambrook <i>et al.</i> , MOLECULAR CLONING: A LABORATORY MANUAL, Cold Spring Harbor Laboratory Press, New York (2d ed. 1989), Vol. II, pp. 15.51-15.113	
80	Schrijver et al., "Comparison of DNA application methods to reduce BRSV shedding in cattle," Vaccine 16(2-3):130-4 (1998)	
81	Simmons et al., "Potent inhibition of HIV-1 infectivity in macrophages and lymphocytes by a novel CCR5 antagonist," Science 276:276-9 (1997)	
82	Stern et al., Chap. 4, Interleukin-12, in Human Cytokines: Handbook for Basic and Clinical Research 74-96 (Aggarwal & Gutterman eds., 1996)	
83	Tan et al., "Characterization of IL-10 Receptors on Human and Mouse Cells," J. Biol. Chem. 268(28):21053-59 (1993)	
84	Thomas et al., "Potent interleukin 3 receptor agonist with selectively enhanced hematopoietic activity relative to recombinant human interleukin 3," PNAS USA 92:3779-83 (1995)	
85	Tuite, "Strategies for the genetic manipulation of Saccharomyces cerevisiae," Crit. Rev. Biotechnol. 12(1-2):157-88 (1992)	
86	Udagawa et al., "Interleukin-18 (interferon-gamma-inducing factor) is produced by osteoblasts and acts via granulocyte/macrophage colony-stimulating factor and not via interferon-gamma to inhibit osteoclast formation," J. Exp. Med. 185(6):1005-12 (1997)	
87	Ulrich et al., "Chimeric HBV core particles carrying a defined segment of Puumala hantavirus nucleocapsid protein evoke protective immunity in an animal model," Vaccine 16(2-3):272-80 (1998)	
88	Villbrandt et al., "Investigations of the thermostability and function of truncated <i>Thermus aquaticus</i> DNA polymerase fragments," <i>Protein Eng'g</i> 10(11):1281-88 (1997)	
89	Weiner et al., "Immunostimulatory oligodeoxynucleotides containing the CpG motif are effective as immune adjuvants in tumor antigen immunization," PNAS USA 94:10833-7 (1997)	
90	Yao et al., "Human IL-17: A Novel Cytokine Derived from T Cells," J. Immunol. 155(12):5483-86 (1995)	
91	York et al., "Antigen processing and presentation by the class I major histocompatibility complex," Annu. Rev. Immunol. 14:369-96 (1996)	
92	Yoshie et al., "Novel lymphocyte-specific CC chemokines and their receptors," J. Leukocyte Biol. 62(5):634-44 (1997)	
93	Zaremba et al., "Identification of an enhancer agonist cytotoxic T lymphocyte peptide from human carcinoembryonic antigen," Cancer Res. 57(20):4570-77 (1997)	

	d	
Examiner	Date	
Signature	Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

REFERENCES CITED IN APPENDIX \mathbb{C}^1

Ref. #	Reference	Claim(s)
1*	Alcami <i>et al.</i> , "A soluble receptor for interleukin-1 beta encoded by vaccinia virus: a novel mechanism of virus modulation of the host response to infection," <i>Cell</i> 71(1): 153-67 (1992)	42
2*	Apostolopoulos et al., "Breast cancer immunotherapy: Current status and future prospects," <i>Immunol. and Cell. Biol.</i> 74: 457-64 (1996)	76
3*	Atamas <i>et al.</i> , "An alternative splice variant of human IL-4, IL-4 delta 2, inhibits IL- 4-stimulated T cell proliferation," <i>J. Immunol.</i> 156(2): 435-41 (1996)	43
4*	Aversa et al., "SLAM and its role in T cell activation and Th cell responses." Immunol. Cell Biol. 75(2): 202-5 (1997)	31
5*	Bach et al., "The IFN gamma receptor: a paradigm for cytokine receptor signaling," Annu. Rev. Immunol. 15: 563-91 (1997)	42
6*	Baggioloni et al., Annu. Rev. Immunol. 15: 675-705, 675 (1997)	12, 14, 41
7*	Baggioloni et al., Annu. Rev. Immunol. 15:675-705, 676 (1997)	15
8*	Balbas et al., "Design and Construction of Expression Plasmid Vectors in Escherichia coli," in METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY, Vol. 185, pp. 14-37 (David V. Goeddel ed., Acad. Press, 1991)	49, 62
9*	Basham et al., "Synergistic antitumor activity with IFN and monoclonal anti-idiotype for murine B cell lymphoma. Mechanism of action," J. Immunol. 141(8): 2855-60 (1988)	37
10*	Beck et al., "Analysis of Multiple Plasmodium falciparum Infections in Tanzanian Children during the Phase II Trial of Malaria Vaccine SPf66," J. Inf. Disease 175: 921-26 (1997)	79

The references indicated with an asterisk ("*") are attached with this list. The remaining references were previously submitted in a separate Information Disclosure Statement.

Ref. #	<u>Reference</u>	Claim(s)
11*	Becket et al., "Characterization of a Prostate Carcinoma Mucin-Like Antigen (PMA)," Int. J. Cancer 62: 703-10 (1995)	76
12*	Bramson <i>et al.</i> , "Construction of a double recombinant adenovirus vector expressing a heterodimeric cytokine: in vitro and in vivo production of biologically active interleukin-12," <i>Hum. Gene Ther.</i> 7(3): 333-42 (1996)	36
13*	Brusselle <i>et al.</i> , "Role of IFN-γ in the Inhibition of Allergic Airway Inflammation Caused by IL-12," <i>Am. J. Respir. Cell Mol. Biol.</i> 17: 767-71 (1997)	25, 26
14*	Censini et al., "cag, a pathogenicity island of Helicobacter pylori, encodes type I-specific and disease-associated virulence factors," PNAS USA 93: 14648-53 (1996)	77
15*	Chen et al., "Discontinuous epitopes of hepatitis B surface antigen derived from a filamentous phage peptide library," PNAS USA 93(5): 1997-2001 (1996)	23
16*	Chow et al., "Improvement of Hepatitis B Virus DNA Vaccines by Plasmids Coexpressing Hepatitis B Surface Antigen and Interleukin-2," J. Virol. 71(1): 169-78 (1997)	20
17*	Ciernik et al., "Induction of Cytotoxic T Lymphocytes and Antitumor Immunity with DNA Vaccines Expressing Single T Cell Epitopes," J. Immunol. 156: 2369-75 (1996)	81, 82
18*	Cohen et al., "Host factors in the pathogenesis of HIV disease," Immunol. Rev. 159:31-48 (1997)	15
19*	Cortese et al., "Selection of biologically active peptides by phage display of random peptide libraries," Curr. Opin. Biotechnol. 7(6): 616-21 (1996)	19
20*	Crameri et al., "DNA Shuffling of a Family of Genes From Diverse Species Accelerates Directed Evolution," Nature 391: 288-91 (1998)	75
21*	Curtis et al., "Recombinant Soluble Interleukin-11 (IL-11) Receptor alpha Chain Can Act as an IL-11 Antagonist," Blood 90(11): 4403-12 (1997)	42

Ref. #	Reference	Claim(s)
22	Cwirla et al., "Peptides on phage: A vast library of peptide for identifying ligands," PNAS USA 87:6378-6382 (1990)	16, 17, 37
23*	Cwirla et al., "Peptide Agonist of the Thrombopoietin Receptor as Potent as the Natural Cytokine," Science 276: 1696-9 (1997)	12, 16
24*	Dagan <i>et al.</i> , "High level expression and production of recombinant human interleukin analogs," <i>Protein Exp. Purif.</i> 3(4): 290-4 (1992)	59, 60
25*	Devos et al., "Interleukin-5 and its receptor: a drug target for eosinophilia associated with chronic allergic disease," J. Leukoc. Biol. 57(6): 813-19 (1995)	26
26*	de Vries et al., Interleukin-4 and Interleukin-13, Chap. 8, in CYTOKINE REGULATION OF HUMORAL IMMUNITY: BASIC AND CLINICAL ASPECTS 195-215 (C. M. Snapper, West Sussex, UK, John Wiley and Sons, 1996)	26
27*	de Vries et al., "Modulation of the human IgE response," Eur. Respir. J. Suppl. 22: 58s-62s (1996)	26
28*	de Vries et al., "Novel fundamental approaches to intervening in IgE-mediated allergic diseases," J. Invest. Dermatol. 102(2): 141-4 (1994)	26
29*	De Waal Malefyt et al., "A Novel Cytokine Belonging to the IL-10 Gene Family Affects Human Monocytes and T Cells," Abstract, 13th European Immunology Meeting, Amsterdam, Netherlands, June 1997, Immunol. Letters 56(1): 211 (1997)	28, 33, 84
30*	Donnelly et al., "DNA Vaccines," Annu. Rev. Immunol. 15: 617-48, 620 (1997)	8, 20, 21, 22, 49, 51, 52
31*	Dudler et al., "A Link Between Catalytic Activity, IgE-Independent Mast Cell Activation and Allergenicity of Bee Venom Phospholipase A ₂ ," J. Immunol. 155(5): 2605-13 (1995)	46
32	Dunn, "Phage display of proteins," Curr. Opin. Biotechnol. 7(5): 547-53 (1996)	19

Ref. #	<u>Reference</u>	Claim(s)
33*	Eckhart <i>et al.</i> , "Immunogenic presentation of a conserved gp41 epitope of human immunodeficiency virus type 1 on recombinant surface antigen of hepatitis B virus," <i>J. Gen. Virol.</i> 77 (9): 2001-8 (1996)	56, 58
34*	Fomsgaard et al., "Improved humoral and cellular immune response against the gp120 V3 loop of HIV-1 following genetic immunization with a chimeric DNA vaccine encoding the V3 inserted in the hepatitis B surface antigen," Scand. J. Immunol. 47(4): 289-95 (1998)	56, 58
35*	Foy et al., "Immune regulation by CD40 and its ligand GP39," Annu. Rev. Immunol. 14: 591-617 (1996)	31
36*	Fromm <i>et al.</i> , "Expression of genes transferred into monocot and dicot plant cells by electroporation." <i>PNAS USA</i> 82(17): 5824-8 (1985)	65, 66
37	Gaczynska <i>et al.</i> , "Proteasome subunits X and Y alter peptidase activities in opposite ways to the interferon-gamma-induced subunits LMP2 and LMP7," <i>J. Biol. Chem.</i> 271(29): 17275-80 (1996)	55
38*	Gauchat et al., "Regulation of human IgE synthesis: the role of CD4+ and CD8+ T-cells and the inhibitory effects of interferonalpha." Eur. Respir. J. Suppl. 13: 31s-38s (1991)	26
39*	Goff et al., "Laboratory Methods: Efficient Saturation Mutagenesis of a Pentapeptide Coding Sequence Using Mixed Oligonucleotides," DNA 6(4):381-388 (1987)	9, 67, 69, 71
40*	Greenfeder et al., "Insertion of a Structural Domain of Interleukin (IL)-1B Confers Agonist Activity to the IL-1 Receptor Antagonist," J. Biol. Chem. 270(38): 22460-66 (1995)	12, 41
41*	Grewal et al., "The CD40-CD154 system in anti-infective host defense," Curr. Opin. Immunol. 9(4): 491-7 (1997)	31
42	Groettrup <i>et al.</i> , "The subunits MECL-1 and LMP2 are mutually required for incorporation in the 20S proteasome," <i>PNAS USA</i> 94: 8970-5 (1997)	55

Ref. #	Reference	Claim(s)
43*	Grunig <i>et al.</i> , "Interleukin-10 is a natural suppressor of cytokine production and inflammation in a murine model of allergic bronchopulmonary aspergillosis," <i>J. Exp. Med.</i> 185(6): 1089-99 (1997)	26
44	Han et al., PNAS USA 92:9747-9751 (1995)	17
45*	Hannum <i>et al.</i> , "Interleukin-1 receptor antagonist activity of a human interleukin-1 inhibitor," <i>Nature</i> 343(6256): 336-40 (1990)	41
46*	Hathcock <i>et al.</i> , "Comparative Analysis of B7-1 and B7-2 Costimulatory Ligands: Expression and Function," <i>J. Exp. Med.</i> 180: 631-40 (1994)	40
47*	Herz et al., "Molecular approaches to receptors as targets for drug discovery," J. Recept. Signal Transduct. Res. 17(5): 671-776 (1997)	35
48*	Hess et al., "Superior efficacy of secreted over somatic antigen display in recombinant Salmonella vaccine induced protection against listeriosis," PNAS USA 93: 1458-63 (1996)	77
49*	Hill et al., "Mutagenesis with Degenerate Oligonucleotides: An Efficient Method for Saturating a Defined DNA Region with Base Pair Substitutions," in METHODS IN ENZYMOLOGY: RECOMBINANT DNA 155: 558-568 (Ray Wu ed., Acad. Press, Inc., 1987)	9, 67, 69, 71
50*	Horuk, TIPS 15: 159-165, 159 (1994)	14
51*	Horwitz et al., in Methods in Enzymology: Gene Expression Technology 185: 599-611 (David V. Goeddel ed., Acad. Press, Inc. 1990)	9
52*	HUMAN CYTOKINES: HANDBOOK FOR BASIC AND CLINICAL RESEARCH, Vol. II (Aggarwal & Gutterman eds. 1996)	14
53*	HUMAN CYTOKINES: HANDBOOK FOR BASIC AND CLINICAL RESEARCH, Vols. I-II (Aggarwal & Gutterman eds. 1996)	33, 39, 83, 84
54*	Ihle et al., "Signaling through the hematopoietic cytokine receptors," Annu. Rev. Immunol. 13: 369-98 (1995)	34

Application No.: 09/724,869
Attorney Docket No.: 0155.130US
(formerly 18097-030310US)
BDSM Docket No.: 032705-006

Ref. #	<u>Reference</u>	Claim(s)
55	Jiang et al., "Subtraction hybridization identifies a novel melanoma differentiation associated gene, mda-7, modulated during human melanoma differentiation, growth and progression," Oncogene 11(12): 2477-86 (1995)	28, 33, 84
56*	Kaufman, "Vectors Used for Expression in Mammalian Cells," in METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY, Vol. 185, pp. 487-511 (David V. Goeddel ed., Acad. Press, 1991)	49, 63
57*	Kay et al., Phage Display of Peptides and Proteins: A Laboratory Manual (Academic Press 1996)	18, 37
58	Kim et al., "In Vivo Engineering of a Cellular Response by Coadministration of IL-12 Expression Vector with a DNA immunogen," J. Immunol. 158(2):816-26 (1997)	8, 36
59	Klinman et al., "Contribution of CpG Motifs to the Immunogenicity of DNA Vaccines," J. Immunol. 158(8): 3635-39 (1997)	24
60*	Krieger et al., "Structures and functions of multiligand lipoprotein receptors: macrophage scavenger receptors and LDL receptor-related protein (LRP)," Annu. Rev. Biochem. 63: 601-37 (1994)	13
61*	Kroemer et al., "Immunoregulation by cytokines," Crit. Rev. Immunol. 13(2): 163-91 (1993)	32, 34
62*	Laberge et al., J. Immunol. 156(1): 310-5 (1996)	33, 84
63*	Le Borgne et al., "In Vivo Induction of Specific Cytotoxic T Lymphocytes in Mice and Rhesus Macaques Immunized with DNA Vector Encoding an HIV Epitope Fused with Hepatitis B Surface Antigen," Virology 240: 304-15 (1998)	56, 58
64*	Le Grice, "Regulated Promoter for High-Level Expression of Heterologous Genes for <i>Bacillus subtilis</i> ," in METHODS IN ENZYMOLOGY: GENE EXPRESSION TECHNOLOGY, Vol. 185, pp. 201-214 (David V. Goeddel ed., Acad. Press, 1991)	49, 62
65*	Levinson, "Expression of Heterologous Genes in Mammalian Cells," in Methods in Enzymology: Gene Expression Technology, Vol. 185, pp. 485-4871 (David V. Goeddel ed., Acad. Press, 1991)	49, 63

Ref. #	Reference	Claim(s)
66*	Livnah et al., "Functional Mimicry of a Protein Hormone by a Peptide Agonist: The EPO Receptor Complex at 2.8," Science 273: 464-71 (1996)	12, 16
67*	Ma et al., "Antibody production and engineering in plants," Ann. NY Acad. Sci. 792: 72-81 (1996)	64
68*	Mattion et al., "Characterization of recombinant polioviruses expressing regions of rotavirus VP4, hepatitis B surface antigen, and herpes simplex virus type 2 glycoprotein D," J. Virol. 69: 5132-37 (1995)	78
69*	McLafferty et al., "M13 bacteriophage displaying disulfide- constrained microproteins," Gene 128(1): 29-36 (1993)	19
70*	Miele, "Plants as bioreactors for biopharmaceuticals: regulatory considerations," <i>Trends Biotechnol.</i> 15(2): 45-50 (1997)	64
71*	Mosmann et al., "Heterogeneity of Cytokine Secretion Patterns and Functions of Helper T cells," Adv. Immunol. 46: 111-147 (1989)	38, 44, 45
72*	Murray et al., "Saturation mutagenesis of a major histocompatibility complex protein domain: Identification of a single conserved amino acid important for allorecognition," PNAS USA 85:3535-39 (1988)	9, 67, 69, 71
73*	Noguchi et al., "IgE responsiveness to Dermatophagoides farinae in young asthmatic children: IgE binding study using recombinant allergens of Der f1, Der f2 and mutant proteins of Der f2," Int. Arch. Allergy Immunol. 110(4): 380-7 (1996)	46
74*	Ostermeier et al., "Combinatorial protein engineering by incremental truncation," PNAS USA 96: 3562-67 (1999)	73
75*	Ostermeier et al., "A combinatorial approach to hybrid enzymes independent of DNA homology," Nature 19: 1205-09 (1999)	73
76*	Parronchi <i>et al.</i> , "IL-4 and IFN (α and γ) exert opposite regulatory effects on the development of cytolytic potential by Th1 or Th2 human T cell clones," <i>J. Immunol.</i> 149(9): 2977-83 (1992)	26, 38, 39

Ref. #	Reference	Claim(s)
77	Paul et al., "Lymphocyte responses and cytokines," Cell 76: 241-251, 241-242 (1994)	12, 14, 38, 39, 41, 44, 45, 83
78*	Paul, The Immune System: An Introduction, Chap. 1, pp. 1-20 in FUNDAMENTAL IMMUNOLOGY (W. E. Paul. New York, Raven Press, 1993)	81, 82
79	Pisetsky, "Immune Activation by Bacterial DNA: A New Genetic Code," <i>Immunity</i> 5: 303-10 (1996)	24
80*	Porcelli, "The CD1 family: a third lineage of antigen-presenting molecules," <i>Adv. Immunol.</i> 59: 1-98 (1995)	31
81*	Premack et al., Nature Med. 2(11): 1174-1178, 1174 (1996)	14
82*	Pumpens et al., "Hepatitis B virus core particles as epitope carriers," Intervirology 38(1-2): 63-74 (1995)	22
83*	Quaratino <i>et al.</i> , "Similar antigenic surfaces, rather than sequence homology dictate T-cell epitope molecular mimicry," <i>PNAS USA</i> 92: 10398-402 (1995)	80
84*	Randhawa <i>et al.</i> , "In vitro culture of B-lymphocytes derived from Epstein-Barr-virus-associated posttransplant lymphoproliferative disease: cytokine production and effect of interferon-alpha," <i>In Vitro Cell Dev Biol Anim.</i> 33(10): 803-8 (1997)	37
85*	Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, New York (2d ed. 1989)	46, 47, 54, 74, 85, 86
86*	Sambrook et al., MOLECULAR CLONING: A LABORATORY MANUAL, Cold Spring Harbor Laboratory Press, New York (2d ed. 1989), pp. 1.53-1.59	7
87*	Sambrook <i>et al.</i> , MOLECULAR CLONING: A LABORATORY MANUAL Cold Spring Harbor Laboratory Press, New York (2d ed. 1989) pp. 15.51-15.113	9

Ref. #	<u>Reference</u>	Claim(s)
88	Sayers et al., "5'-3' Exonucleases in phosphorothioate-based oligonucleotide-directed mutagenesis," Nucleic Acids Res. 16: 791-802 (1988)	73
89*	Schrijver <i>et al.</i> , "Comparison of DNA application methods to reduce BRSV shedding in cattle," <i>Vaccine</i> 16(2-3): 130-4 (1998)	52
90*	Simmons et al., "Potent inhibition of HIV-1 infectivity in macrophages and lymphocytes by a novel CCR5 antagonist," Science 276 (5310):276-9 (1997)	15
91	Stemmer, "Searching Sequence Space," <i>Biotechnology</i> 13: 549-53 (1995)	75
92*	Stern et al., Chap. 4, Interleukin-12, in Human Cytokines. Handbook for Basic and Clinical Research 74-96 (Aggarwal & Gutterman eds., 1996)	26
93	Stohwasser <i>et al.</i> , "Molecular cloning of the mouse proteasome subunits MC14 and MECL-1: reciprocally regulated tissue expression of interferon-gamma-modulated proteasome subunits," <i>Eur. J. Immunol.</i> 27(5): 1182-7 (1997)	55
94*	Tan et al., "Characterization of recombinant extracellular domain of human interleukin-10 receptor." J. Biol. Chem. 270(21): 12906-11 (1995)	27, 28, 43
95	Tan et al., "Characterization of IL-10 Receptors on Human and Mouse Cells," J. Biol. Chem. 268(28): 21053-59 (1993)	27
96*	Thomas et al., "Potent interleukin 3 receptor agonist with selectively enhanced hematopoietic activity relative to recombinant human interleukin 3," PNAS USA 92: 3779-83 (1995)	12
97*	Tuite, "Strategies for the genetic manipulation of Saccharomyces cerevisiae," Crit. Rev. Biotechnol. 12(1-2): 157-88 (1992)	63
98*	U.S. Pat. No. 6,376,246	68, 69, 70, 72
99	U.S. Pat. No. 5,571,698, col. 48, ll. 45-65	19

Application No.: 09/724,869
Attorney Docket No.: 0155.130US
(formerly 18097-030310US)
BDSM Docket No.: 032705-006

Ref. #	<u>Reference</u>	Claim(s)
100	U.S. Pat. No. 5,571,698, col. 7, 1l. 37-38 and col. 47, l. 65 to col. 48, l. 22	18
101	U.S. Pat. No. 5,571,698	17
102	U.S. Pat. No. 5,348,867	18
103*	Udagawa <i>et al.</i> , "Interleukin-18 (interferon-gamma-inducing factor) is produced by osteoblasts and acts via granulocyte/macrophage colony-stimulating factor and not via interferon-gamma to inhibit osteoclast formation," <i>J. Exp. Med.</i> 185(6): 1005-12 (1997)	33, 84
104*	Ulrich et al., "Chimeric HBV core particles carrying a defined segment of Puumala hantavirus nucleocapsid protein evoke protective immunity in an animal model," <i>Vaccine</i> 16(2-3): 272-80 (1998)	22
105*	Villbrandt et al., Protein Eng'g 10(11): 1281-88 (1997)	50
106*	Weiner et al., "Immunostimulatory oligodeoxynucleotides containing the CpG motif are effective as immune adjuvants in tumor antigen immunization," PNAS USA 94: 10833-7 (1997)	24
107	WEIR'S HANDBOOK OF EXPERIMENTAL IMMUNOLOGY (Leonore A. Herzenberg <i>et al.</i> eds., 5 th ed. 1996)	85, 86
108	WO 99/41383	48, 50
109	WO 99/41369	49, 50
110	WO 99/41368	9-11
111	WO 99/23107	48, 50, 73
112	WO 98/27230	9-11, 48, 50, 74
113*	WO 94/18330	17
114*	WO 94/01567	17
115*	WO 92/18619	19

Application No.: 09/724,869
Attorney Docket No.: 0155.130US
(formerly 18097-030310US)
BDSM Docket No.: 032705-006

Ref. #	Reference	Claim(s)
116	WO 92/06204	19
117*	WO 92/01047	19
118*	WO 91/19818	19
119*	Yao et al., "Human IL-17: A Novel Cytokine Derived from T Cells," J. Immunol. 155(12): 5483-6 1995	33, 84
120*	York et al., "Antigen processing and presentation by the class I major histocompatibility complex," Annu. Rev. Immunol. 14: 369-96 (1996)	55, 56
121*	Yoshie et al., "Novel lymphocyte-specific CC chemokines and their receptors," J. Leukoc. Biol. 62(5): 634-44 (1997)	15, 65, 66
122*	Zaremba <i>et al.</i> , "Identification of an enhancer agonist cytotoxic T lymphocyte peptide from human carcinoembryonic antigen," <i>Cancer Res.</i> 57(20): 4570-7 (1997)	58, 80